

Office Action Summary

Application No.

08/950,542

Applicant(s)

Bachovchin

Examiner

David Lukton

Art Unit

1653



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on Aug 17, 2001

2a) ☒ This action is **FINAL**.

2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 35 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 35-51 is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 35-51 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirements.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d)

a) ☐ All b) ☐ Some* c) ☐ None of

1 Certified copies of the priority documents have been received.

2 Certified copies of the priority documents have been received in Application No. _____.

3 Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

15) ☐ Information Statement (PCT-M409) Paper(s) _____

16) ☐ Information Statement (PCT-M409) Paper(s) _____

17) ☐ Information Statement (PCT-M409) Paper(s) _____

18) ☐ Other _____

Pursuant to the directives of paper No. 48 (filed 8/17/01), claims 35 and 42 have been amended. Claims 35-51 remain pending.

Applicants' arguments filed 1/26/01 have been considered and found not persuasive.

✱

The following is a quotation of the first paragraph of 35 U.S.C. §112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 35-51 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicants have not enabled one to obtain the requisite isomer with a purity of 96% or greater. As asserted by applicants, the procedure on page 15, lines 3-11 does not work and leads to an erroneous conclusion. As for the procedure on page 21, only the L,L and L,D isomers are referred to. As explained by applicants, there are four different isomers:

cis-L-Ala-D-boroPro and *trans*-L-Ala-D-boroPro

cis-L-Ala-L-boroPro and *trans*-L-Ala-L-boroPro.

This is not a chemical structure.

The situation is further complicated by

interconversion of one or more isomers to other isomers under certain circumstances not explained in the specification. Accordingly, one would have to "know" that (a) the procedure on page 15, lines 3+ must be ignored, and (b) the procedure on page 21 is incomplete, and could easily lead to erroneous results. It is not enough to say that this or that isomer comes of "first", when in fact the term "L,L" really refers, in hindsight to a mixture of *cis*-L,L and *trans*-L,L; similarly the term "L,D" really refers, in hindsight, to a mixture of *cis*-L,D and *trans*-L,D isomers. Thus, the specification does not enable one to "make and use" the claimed invention. Moreover, even if it were true that enablement exists for purifying the compounds *cis*-L-Ala-L-boroPro and *trans*-L-Ala-L-boroPro, the claims encompass an infinite number of compounds, of size ranging from two amino acids to 2 million, and of polarities that cover the entire spectrum of highly lipophilic to highly hydrophilic. Even if applicants could make the argument that the procedure is clear for this one compound (which it is not), the issue of the *cis* and *trans* isomers would have to be dealt with for many of the remaining compounds in the genus.

In response to the foregoing, applicants have attempted to dismiss the significance of the *cis*/*trans* isomerization problem by arguing the claims encompass both. It may be true that the claims encompass both, but that is not the issue. The issue instead is that of overcoming the purification challenges which these various isomers impose.

Applicants have argued that it does not matter if

procedure which is accurately described. However, the fact that specification contains experimental direction and guidance which is erroneous and misleading would confuse the skilled chemist.

The rejection is maintained.

✱

Claims 35-51 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Each of claims 35 and 42 recites that the stereochemical purity of the carbon atom bearing boron exceeds 96%. However, there does not appear to be support for this number. Similarly, claims 37-39 recite stereochemical purities of 97%, 98% and 99% respectively. Again, there is no support for this in the specification. In response, applicants have pointed to the following passage on page 21:

"...achieved an isomeric purity of about 99-6% for each isomer."

While there appears to be agreement that "99-6%" is an obvious error, there is no agreement about what was intended in its place or what the skilled chemist would believe was intended. Applicants are now making the argument that the designation "99-6%" really means 99-96%. However, this appears unlikely.

Application was not reheard.

from Japanese, Hebrew, Spanish, or any other foreign language; the writer of the specification would have written 96 - 99%, if that had been intended, rather than 99-96%. It is more likely that what was intended by the designation "99-6%" was 99.6%, i.e., a decimal point rather than a hyphen. But even this is not a certainty. Whatever the analysis, any conclusion based on the contested designation is tenuous at best.

After asserting that support exists for the percentage of 96% (a point which is very much in dispute), applicant next argues that support for higher percentages, up to, but not including 100% is implied because a chemist would want to achieve higher purity. Perhaps a chemist would want this, and perhaps not. But there is no recitation of any percentage between 96 and 100%. Applicants go on to state: "Therefore, other percentages in the range of 95% to 100% would be understood ...". However, the location in the text where applicants have obtained the 95% figure has not been disclosed. It is assumed to be absent, unless identified by applicants. As for the 100% figure, the claims specifically exclude this. The claims mandate the presence of at least two compounds; accordingly, the percentage of any one compound is necessarily less than 100%. Thus, neither the 95% figure nor the 100% figure is supported by the specification and claims.

Next, applicants have pointed to *In re Johnson* (194 USPQ 187) which pertained to an application which matured into USP 4,108,837. As applicants have indicated, the Court did permit the applicant to exclude two compounds which were not disclosed in the

differences between that and the instant case. First, the *Johnson* case pertained to specific structures of organic compounds; in the instant case, numbers are at issue. Applicants have attempted to frame the issue (of the range of numbers) in terms of integers; of course, this is misleading. There is no statement or suggestion that only integers are included. From the perspective of a mathematician, there are an infinite number of "data points" between 96% and 100%. Admittedly, an analytical chemist would have a different view of this; the chemist would have to contend to the limits of instrumental detection and discrimination. An analytical chemist might argue that going beyond two decimal places (1/100 of a percentage point) is counterproductive, and that only the following should be considered: 96.00, 96.01, 96.02, 96.03, 96.04, 96.05, etc. Pursuing this line of logic, there would be 400 "data points" between 96% and 100%. Thus, in attempting to apply the *In re Johnson* decision, one would have to exclude, not single data points, but ranges of data points. Further, the "new matter" issue has not been revisited by the appellate court subsequent to issuance of *In re Baird* (29 USPQ2d 1550, 1994); the court may decide that a consistent policy should apply both to applicants seeking to exclude subject matter, and examiners endeavoring to exclude a portion of a genus in applying a §103 rejection. In addition to the foregoing, in the instant case, the upper and lower limits of the percentages are undefined, contrary to applicants' assertions; i.e., neither the point 95% nor the point 96% is recited in the specification, and the "point" 100% is not recited in the specification.

is the range confined to 95 - 100% as applicants would argue, or does it extend to e.g., 0.0001% to 99.999%, or is it some other range? None of this is clear from the specification. If the disclosed range is 0.01% to 99.99%, then 96,000 data points would have to be excluded. And even if there were support in the specification for the range of 95% - 99.99% (and there is not), applicants would still have to exclude 100 "data points" to arrive at the claimed genus. Thus, it is not apparent that *In re Johnson* is controlling in the instant case. The rejection is maintained.

As indicated previously, there is another issue which is somewhat related to the foregoing, but is distinct therefrom. Claims 35 and 42 make reference to a mixture of stereoisomers, as well as a lower limit of two. If the claim is going to recite, or imply that there are at least two stereoisomers, applicants will have to point to a page and line number in the specification where support may be found. Note that even if page 21 had recited that the "isomeric purity" of each isomer were 96% (rather than 99-6%), this would not support the lower limit of two stereoisomers, or for that matter two isomers. Thus, applicants should point to the page and line number where the lower limit of two stereoisomers is recited; in addition, applicants should point to the page and line number where a mixture of any number of stereoisomers is recited for a genus of compounds, as opposed to a specie. This ground of rejection was raised in the last Office action, and applicants have thus far declined comment. This ground of rejection is maintained.

Claims 35-51 are rejected under 35 U.S.C. §112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Each of claims 35 and 42 recites the phrase "capable of being hydrolyzed". However, this renders the claims indefinite as to whether the hydrolysis occurs at all. In response, applicants have argued that if one examiner abstains from imposing a rejection in a particular situation, then all other examiners are subsequently barred from imposing a rejection in a similar situation. However, applicants are not correct on this point. The rejection is maintained.

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The following is a quotation of 35 USC §103 which forms the basis for all obviousness rejections set forth in the Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made, absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103.

(*J. Biol. Chem.* **265**, 3738, 1990).

As indicated previously, Bachovchin teaches (page 3743, col 1, paragraph 3) acquisition of the requisite isomer, but that the purity was only 95%. If the requisite isomer can be obtained with 95% purity after only one pass through a column, then surely a purity in the range of 96 - 99.9% could be obtained after two passes.

In their most recent response (filed 8/17/01), applicants have made no mention of the information in the indicated paragraph on page 3743. Given this teaching, one of ordinary skill could have readily arrived at the claimed invention without any modifications in procedure whatsoever, other than to pass the mixture through the column twice.

The rejection is maintained.

*

Claims 35-51 are rejected under 35 U.S.C. §103 as being unpatentable over Bachovchin (USP 4,935,493) or Bachovchin (WO 89/03223) or Flentke (*Proc Natl Acad Sci* **88**, 1556, 1991).

The teachings of the references were indicated previously. Applicants have argued that (a) a chemist would have no motivation to obtain a pure compound, (b) a chemist would have been unaware of chromatography techniques to purify compounds, and (c) if a chemist tried to purify the stereoisomers of the cited references, the probability of failure would be high.

Applicants have also argued that the

L-isomers are naturally occurring, and in the vast majority of cases, are more active than the corresponding D-isomers.

Applicants have also argued that if a chemist only had possession of a C₁₈ HPLC column, he would not undertake the separation because the probability of failure is so high. Applicants have also argued that the organic chemist of ordinary skill would believe that thin layer chromatography generally provides much better resolution than HPLC. In response, TLC never provides provides better resolution than HPLC. Applicants have also argued that the organic chemist of ordinary skill would believe that fractional crystallization generally provides better separations than than HPLC. However, this is almost never true; fractional crystallization is a "blunt instrument" and was relied upon in the early days of chemistry only because HPLC was not available.

A key point here is that the claims are not drawn to a method of purifying a compound. The claims are drawn primarily to a single pure compound, with the proviso that a finite quantity of impurity must be present. The organic chemist of ordinary skill would have had the motivation to prepare a pure compound, and the means to achieve it.

The rejections are maintained.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). The practice of automatically extending the shortened statutory period an additional month upon filing of a timely first response is hereby discontinued.

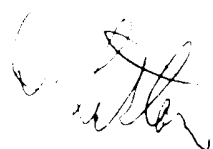
A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED AND ANY EXTENSION FEE PURSUANT TO 37 CFR 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

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No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is (703) 308-3213.

An inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.


DAVID LUKTON
PATENT EXAMINER
GROUP 1800